

Amendments to the Claims:

Please cancel claims 2-23 and add new claims 24-53. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method for producing a protein library, comprising the steps of:
 - a) providing a population of RNA molecules, each of which comprises a translation initiation sequence and a start codon operably linked to a protein coding sequence and each of which is operably linked to a peptide acceptor at the 3' end of said protein coding sequence;
 - b) in vitro translating said protein coding sequences to produce a population of RNA-protein fusions; and
 - c) further incubating said population of RNA-protein fusions under high salt conditions, thereby producing a protein library.

2-23. (Canceled)

24. (New) A molecule comprising a nucleic acid portion and a protein portion covalently bound to said nucleic acid portion through a substance having a chemical structure of a member selected from the group consisting of puromycin, 3'-N-aminoacylpuromycin aminonucleoside, and 3'-N-aminoacyladenosine aminonucleoside,

wherein said nucleic acid portion comprises a polymer of nucleoside, and said protein portion is encoded by said nucleic acid portion.

25. (New) The molecule according to claim 24, wherein a 3'-terminal end of the nucleic acid portion and a C-terminal end of the protein portion are bonded with a covalent bond.

26. (New) The molecule according to claim 24 or 25, wherein a 3'-terminal end of the nucleic acid portion covalently bonded to a C-terminal end of the protein portion is puromycin.

27. (New) The molecule according to claim 24, wherein the nucleic acid portion comprises a gene composed of RNA, and a suppressor tRNA bonded to the gene through a spacer.

28. (New) The molecule according to claim 24, wherein the nucleic acid portion comprises a gene composed of RNA, and a spacer composed of DNA and RNA.

29. (New) The molecule according to claim 24, wherein the nucleic acid portion comprises a gene composed of RNA, and a spacer composed of DNA and polyethylene

glycol.

30. (New) The molecule according to claim 24 or 25, wherein a 3'-terminal end of the nucleic acid portion covalently bonded to a C-terminal end of the protein portion is a substance having the ability to bind to the C-terminal of a synthesized protein when protein synthesis is carried out in a cell-free protein synthesis system.

31. (New) The molecule according to claim 24 or 25, wherein a 3' terminal end of the nucleic acid portion covalently bonded to a C-terminal end of the protein portion is 3'-N-aminoacylpuromycin aminonucleoside or 3'-N-aminoacyladenosine aminonucleoside.

32. (New) The molecule according to claim 25, wherein the covalent bond is formed by a cell-free protein synthesis system.

33. (New) A method for constructing the molecule as defined in claim 28, which comprises (a) preparing a DNA containing a gene which has no termination codon, (b) transcribing the prepared DNA into RNA, (c) bonding a chimeric spacer composed of DNA and RNA to a 3'-terminal end of the obtained RNA, (d) bonding, to a 3'-terminal end of the obtained bonded product, a nucleoside or a substance having a chemical structure analogous to that of a nucleoside, which can be covalently bound to an amino

acid or a substrate having a chemical structure analogous to that of an amino acid, and (e) performing protein synthesis in a cell-free protein synthesis system using the obtained bonded product as mRNA to bond a nucleic acid portion containing the gene to a translation product of the gene, thereby constructing the molecule.

34. (New) A method for constructing the molecule as defined in claim 29, which comprises (a) preparing a DNA containing a gene which has no termination codon, (b) transcribing the prepared DNA into RNA, (c) bonding a chimeric spacer composed of DNA and polyethylene glycol to a 3'-terminal end of the obtained RNA, (d) bonding, to a 3'-terminal end of the obtained bonded product, a nucleoside or a substance having a chemical structure analogous to that of a nucleoside, which can be covalently bound to an amino acid or a substance having a chemical structure analogous to that of an amino acid, and (e) performing protein synthesis in a cell-free protein synthesis system using the obtained bonded product as mRNA to bond a nucleic acid portion containing the gene to a translation product of the gene, thereby constructing the molecule.

35. (New) The construction method according to claim 33 or 34, wherein the nucleoside or the substance having the chemical structure analogous to that of the nucleoside is puromycin.

36. (New) A method for protein evolution simulation, which comprises a construction step for constructing molecules from a DNA containing a gene by the construction method as defined in any one of claims 33 and 34, a selection step for selecting the molecules obtained in the construction step, a mutation introduction step for introducing a mutation into a gene portion of a molecule selected in the selection step, and an amplification step for amplifying the gene portion obtained in the mutation introduction step, thereby simulating protein evolution.

37. (New) A method for assaying protein/protein or protein/nucleic acid intermolecular action, which comprises a construction step for constructing molecules by the construction method of any one as defined in claims 33 and 34, and an assay step for examining intermolecular action of the molecules obtained in the construction step with another protein or nucleic acid, thereby assaying protein/protein or protein/nucleic acid intermolecular action.

38. (New) The method for protein evolution simulation according to claim 36, wherein the construction step, the selection step, the mutation introduction step and the amplification step are repeatedly performed by providing the DNA obtained in the amplification step to the construction step.

39. (New) The method for protein evolution simulation according to claim 36, wherein the selection step is conducted using a target substance which is bound to a solid-state surface.

40. (New) A molecule comprising a nucleic acid portion and a protein portion covalently bound to said nucleic acid portion through a substance having a chemical structure of a member selected from the group consisting of puromycin, an analog of puromycin, and 3'-N-aminoacyladenosine aminonucleoside, wherein said nucleic acid portion comprises nucleotides, and said protein portion is encoded by said nucleic acid portion.

41. (New) The molecule of claim 40, wherein said protein portion comprises two or more amino acids joined by one or more peptide bonds.

42. (New) A method for constructing the molecule as defined in claim 40, said method comprising (a) preparing a DNA containing a protein coding sequence; (b) transcribing the DNA into RNA; (c) covalently bonding to the 3' end of the protein coding sequence of the transcribed RNA a chemical structure selected from the group consisting of puromycin, a puromycin analog, and 3'-N-aminoacyladenine aminonucleoside; and (d) translating the RNA in a cell-free protein synthesis system, thereby constructing the molecule of claim 40.

43. (New) The method of claim 42, wherein step (a) comprises synthesizing a DNA primer and a DNA template, and amplifying said DNA template using said DNA primer via polymerase chain reaction.

44. (New) The method of claim 42, wherein said cell-free protein synthesis system in step (d) is a wheat germ system or a reticulocyte system.

45. (New) A method for *in vitro* selection and evolution, wherein said method comprises the steps of:

(a) constructing a first plurality of molecules, wherein each molecule is a molecule according to 40;

(b) selecting one or more molecules from said first plurality, thereby obtaining one

or more first selected molecules;

(c) using the nucleic acid portion of the one or more first selected molecules to mutagenically construct a second plurality of molecules, wherein each molecule is a molecule according to claim 40.

46. (New) The method according to claim 45, further comprising the additional step of selecting one or more molecules from said second plurality, thereby obtaining one or more second selected molecules, wherein the nucleic acid and protein portions of said one or more second selected molecules differ from the nucleic acid and protein portions of said one or more first selected molecule.

47. (New) The method according to claim 45, wherein said selecting steps comprises contacting said first plurality of molecules with a target molecule or immobilized selection motif.

48. (New) The method according to claim 46, wherein said selecting steps are carried out by contacting said first and second plurality of molecules with a target molecule or immobilized selection motif.

49. (New) The method according to any of claims 45-48, wherein step (c)

comprises amplification via mutagenic PCR

50. (New) A method for assaying protein/protein or protein/nucleic acid interaction, which comprises the steps of (a) constructing a molecule according to claim 40, and (b) determining whether said molecule interacts with another protein or nucleic acid, thereby assaying protein/protein or protein/nucleic acid interaction.

51. (New) The method of claim 50, wherein step (b) is carried out by combining the molecule according to claim 40 with an antibody, and determining whether said antibody binds to the protein portion of said molecule.

52. (New) The method according to any of claims 50 and 51, wherein said step (b) comprises an immunoprecipitation reaction.

53. (New) The method according to claim 52, wherein said immunoprecipitation reaction is carried out with a c-myc antibody.

Amendment to the Inventorship:

Change the inventors from “Jack W. Szostak, Richard W. Roberts, and Rihe Liu”
to “Jack W. Szostak and Richard W. Roberts.”

REQUEST FOR INTERFERENCE UNDER 37 C.F.R. § 1.607

By this Amendment, Applicants have added new claims 24-53. Under 37 C.F.R. § 1.607(c), Applicants draw the Examiner's attention to the fact that these new claims correspond exactly or substantially to claims 1-6, 10-12, 15, 16, and 19-23, respectively, of U.S. Patent No. 6,361,943 to Yanagawa et al. ("Yanagawa"), and hereby request an interference with that patent. Applicants propose that the interference be declared with the following count.

Proposed Count 1

A molecule comprising a nucleic acid portion and a protein portion covalently bound to said nucleic acid portion through a substance having a chemical structure of a member selected from the group consisting of puromycin, 3'-N-aminoacylpuromycin aminonucleoside, and 3'-N-aminoacyladenosine aminonucleoside, wherein said nucleic acid portion comprises a polymer of nucleoside, and said protein portion is encoded by said nucleic acid portion.

(Corresponds exactly to Yanagawa claim 1)

or

A molecule comprising a nucleic acid portion and a protein portion covalently bound to said nucleic acid portion through a substance having a chemical structure of a member selected from the group consisting of puromycin, an analog of puromycin, and 3'-N-aminoacyladenosine aminonucleoside, wherein said nucleic acid portion comprises nucleotides, and said protein portion is encoded by said nucleic acid portion.

(Corresponds exactly to Applicants' claim 40)

Comments: Proposed Count 1 alternatively comprises Yanagawa independent claim 1 and Applicants' independent claim 40.

Proposed designation of corresponding claims:

Yanagawa: Claims 1-23.

Applicants: Claims 24-53.